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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/060,048	01/29/2002	Gregory Stephanopoulos	MTV-036.01	6568
25181	7590	07/13/2004	EXAMINER	
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			MAHATAN, CHANNING	
			ART UNIT	PAPER NUMBER
			1631	

DATE MAILED: 07/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/060,048

Applicant(s)

STEPHANOPOULOS ET AL.

Examiner

Channing S Mahatan

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-73 is/are pending in the application.
- 4a) Of the above claim(s) 36-45 and 49-73 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-35 and 46-48 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-73 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☒ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 19 June 2002.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

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DETAILED ACTION

APPLICANTS' ELECTION

Applicants' election with traverse of Group I (claims 1-35 and 46-48; drawn to a method, computer product, and system for use in the analysis of gene or protein expression information) in the reply filed on 26 April 2004 is acknowledged. The traversal is on the ground(s) that the simultaneous examination of Groups I, II, and III would not place an undue search burden on the Examiner because these Groups are classified within the same class. This is not found persuasive because classification does not preclude separate and distinct inventions, wherein the different functions, effects, and modes of operations (as indicated in the 'Restriction/Election Requirement, mailed 22 March 2004) would require a non-coextensive search in non-patent literature, thereby establishing a search burden.

The requirement is still deemed proper and is therefore made FINAL.

Claims 36-45 and 49-73 are withdrawn from further consideration pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim.

CLAIMS UNDER EXAMINATION

Claims herein under examination are claims 1-35 and 46-48.

Claims Rejected Under 35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

NON-STATUTORY SUBJECT MATTER

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 101 because the claimed invention

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is directed to non-statutory subject matter. The claimed invention is directed to a “method for use in the analysis of gene or protein expression information”/“computer product for use in the analyzing gene or protein expression data”/“system”.

M.P.E.P. section entitled “Nonfunctional Descriptive Material” states:

Descriptive material that cannot exhibit any functional interrelationship with the way in which computing processes are performed does not constitute a statutory process, machine, manufacture or composition of matter and should be rejected under 35 U.S.C. 101. Thus, Office personnel should consider the claimed invention as a whole to determine whether the necessary functional interrelationship is provided.

Where certain types of descriptive material, such as music, literature, art, photographs and mere arrangements or compilations of facts or data, are merely stored so as to be read or outputted by a computer without creating any functional interrelationship, either as part of the stored data or as part of the computing processes performed by the computer, then such descriptive material alone does not impart functionality either to the data as so structured, or to the computer. Such “descriptive material” is not a process, machine, manufacture or composition of matter. (Data consists of facts, which become information when they are seen in context and convey meaning to people. Computers process data without any understanding of what that data represents. Computer Dictionary 210 (Microsoft Press, 2d ed. 1994).)

The policy that precludes the patenting of nonfunctional descriptive material would be easily frustrated if the same descriptive material could be patented when claimed as an article of manufacture. For example, music is commonly sold to consumers in the format of a compact disc. In such cases, the known compact disc acts as nothing more than a carrier for nonfunctional descriptive material. The purely nonfunctional descriptive material cannot alone provide the practical application for the manufacture.

Office personnel should be prudent in applying the foregoing guidance. Nonfunctional descriptive material may be claimed in combination with other functional descriptive multi-media material on a computer-readable medium to provide the necessary functional and structural interrelationship to satisfy the requirements of 35 U.S.C. 101. The presence of the claimed nonfunctional descriptive material is not necessarily determinative of nonstatutory subject matter. For example, a computer that recognizes a particular grouping of musical notes read from memory and upon recognizing that particular sequence, causes another defined series of notes to be played, defines a functional interrelationship among that data and the computing processes performed when utilizing that data, and as such is statutory because it implements a statutory process.

M.P.E.P. section entitled “Nonstatutory Subject Matter” (pages 2100-12, Columns 1-2) states:

Claims to processes that do nothing more than solve mathematical problems or manipulate abstract ideas or concepts are more complex to analyze and are addressed below.

If the “acts” of a claimed process manipulate only numbers, abstract concepts or ideas, or signals representing any of the foregoing, the acts are not being applied to appropriate subject matter. Schrader, 22 F.3d at 294-95, 30 U.S.P.Q.2d at 1458-59. Thus, a process consisting solely of mathematical operations, i.e., converting one set of numbers into another set of numbers, does not manipulate appropriate subject matter and thus cannot constitute a statutory process.

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Further, M.P.E.P. section entitled “Statutory Process Claims” (page 2100-15, Column 1-2) states:

A claim that requires one or more acts to be performed defines a process. However, not all processes are statutory under 35 U.S.C. 101. Schrader, 22 F.3d at 296, 30 U.S.P.Q.2d at 1460. To be statutory, a claimed computer-related process must either: (A) result in a physical transformation outside the computer for which a practical application in the technological arts is either disclosed in the specification or would have been known to a skilled artisan (discussed in i) below), or (B) be limited to a practical application within the technological arts (discussed in ii) below). See *Diamond v. Diehr*, 450 U.S. at 183-84, 209 U.S.P.Q. at 6 (quoting *Cochrane v. Deener*, 94 U.S. 780, 787-88 (1877)) (“A [statutory] process is a mode of treatment of certain materials to produce a given result. It is an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing.... The process requires that certain things should be done with certain substances, and in a certain order; but the tools to be used in doing this may be of secondary consequence.”). See also *Alappat*, 33 F.3d at 1543, 31 U.S.P.Q.2d at 1556-57 (quoting *Diamond v. Diehr*, 450 U.S. at 192, 209 U.S.P.Q. at 10). See also *id.* at 1569, 31 U.S.P.Q.2d at 1578-79 (Newman, J., concurring) (“unpatentability of the principle does not defeat patentability of its practical applications”) (citing *O'Reilly v. Morse*, 56 U.S. (15 How.) at 114-19). If a physical transformation occurs outside the computer, a disclosure that permits a skilled artisan to practice the claimed invention, i.e., to put it to a practical use, is sufficient. On the other hand, it is necessary for the claimed invention taken as a whole to produce a practical application if there is only a transformation of signals or data inside a computer or if a process merely manipulates concepts or converts one set of numbers into another.

The instant claims are “mental” processes of performing mathematical operations (manipulation of numbers) applied to a computer. For example, instant claim 1 comprises accessing gene or protein expression data, determining a measure of variability of expression levels. Simply determining variability of expression levels provides no useful information; since there is no further indication (i.e. steps) what the variability of expression levels represents. The computer product and system generates the said “variability of expression levels” (data) without any understanding of what the data represents, wherein the “purely non-functional descriptive material cannot alone provide the practical application for the manufacture”, and is thus non-statutory. The claims do not recite any concrete or tangible results; therefore the claims do not recite statutory subject matter.

Claims Rejected Under 35 U.S.C. § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

LACK OF ENABLEMENT

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in Ex parte Forman, 230 U.S.P.Q. 546 (B.P.A.I. 1986) and reiterated by the Court of Appeals in In re Wands, 8 U.S.P.Q. 2d 1400 at 1404 (C.A.F.C. 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 112, first paragraph. It is acknowledged the claimed invention is directed to a “method for use in the analysis of gene or

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protein expression”/“computer product for use in analyzing gene or protein expression data”/“system”. However, absent is the intended goal that would be achieved through the implementation of the instantly claimed method, computer product, and system. For instance (referring to claim 1), after “determining a measure of variability of the expression levels of each of the gene or protein in the data as a whole” and “determining a measure of the variability of expression levels of each gene or protein within each class of sample” what does the determined variabilities of the measured expression levels intended to represent and what does one do with this information? Further, dependent claim 2 indicates the determination of the difference between these variabilities, however, does not indicate what this information represents and what is one to do with the determined difference (i.e. subsequent steps). Thus, one skilled in the art would not understand what the information means and what to do with the information after the generation of the determined “variability of the expression levels” without an intended goal. No guidance, direction, or examples are provided such that one of ordinary skill in the art would have known how to use the claimed invention.

Claims Rejected Under 35 U.S.C. § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-35 and 46-48 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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VAGUE AND INDEFINITE

Claims 1, 46, 48, and all claims dependent therefrom are indefinite due to the lack of clarity of the claim language failing to recite a final process step, which agrees back with the preamble. The preamble states that it is a “method for use in analyzing gene or protein expression data”/“computer product for use in analyzing gene or protein expression data”/“system”, however, the claim(s) recite a final step of “determining a measure of variability of expression levels of the gene or protein within each class of sample in the data”. There is no indication that of the manner in the method is to be used in the analysis of gene or protein expression as recited in the preamble. While minor details are not required in method/process claims, at least the basic step must be recited in a positive, active fashion. The claim does not set forth the conditions/state when the method, computer product, and system are to be used in the analysis of gene or protein expression data. Clarification of the metes and bounds of the claim is requested via clearer claim wording.

Claim 1 and all claims dependent therefrom recite the limitations “G genes”, “S samples”, and “C classes” which are vague and indefinite. It is unclear what defines “G genes”, “S samples”, and “C classes”. Clarification of the metes and bounds, via clearer claim language, is requested.

Claims 1, 46, 48, and all claims dependent therefrom recite the limitation “classes representing cellular states” which is vague and indefinite. It is unclear what Applicants regard as “cellular states”. Applicants’ can resolve this issue by particularly pointing out what such language is intended to encompass. Clarification of the metes and bounds, via clearer claim language, is requested.

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Claim 22 recite the language “the variance-covariance structure is similar in each class” which is vague and indefinite. The above language implies a criteria or range of values which identifies the variance-covariance structure to be similar in each class. Applicants’ can resolve this issue by particularly pointing out the criteria or range of values that establishes variance-covariance to be similar in each class versus being non-similar. Clarification of the metes and bounds, via clearer claim language, is requested.

Claims 31, 32, and all claims dependent therefrom recite the limitation “determining the contribution of the expression levels of a gene or protein to the discriminant loadings, wherein a gene or protein that contributes significantly to a dimension is a gene or a protein that is related to a cellular state of one or more sample” which is vague and indefinite. It is unclear what Applicants’ regard as a “gene or protein that contributes significantly” wherein such language implies parameters that is indicative of significant contribution to dimension. Further, it is unclear what criteria(s) establishes a gene or protein to be related to a cellular state of one or more sample. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 33 recites the limitation “C-1 dimensions” which is confusing. It is unclear if “C-1” is intended to represent a “C dash 1” dimensions or “C minus 1” dimensions or some other “C” dimensions. Applicants can resolve this issue by particularly pointing out the intended language of such limitation. Clarification of the metes and bounds, via clearer claim language, is requested.

Claim 35 recites the language “F score” which is vague and indefinite. It is unclear what Applicants’ regard the “F score” to be defined as/represent, wherein there appears to be no

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definition or criteria for such language throughout the specification. Clarification of the metes and bounds, via clearer claim language, is requested.

Claims Rejected Under 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6, 9-11, and 46-48 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kerr et al.

Kerr et al. describes the analysis of variance for gene expression data taken from microarray (Title). The authors indicate the method can be used to normalize microarray data and provide estimates of changes in gene expression that are corrected for potential confounding effects (claim 1; Abstract; page 820, lines 19-22). Kerr et al. determine the variances of the expression data, determines the differences in variances, determines the ratios of said differences, and scales said measures (claims 2-6 and 9; pages 820-824, beginning on line 24). Further, the authors indicate the calculation of variances may be performed to the g^{th} gene (i.e. wherein G is one or greater) (claims 10 and 11; page 820, lines 27-34). All computations for data analysis were carried out using Matlab software (claims 46-48 (i.e. computer product and processor); page 835, lines 26-28). Thus, Kerr et al. anticipates the claimed invention.

EXAMINER COMMENT

The limitation “Wilks’ lambda score” (claim 7) is understood to mean “the ratio of the “within group variance” to the “total variance” (page 66, lines 17-19 of the Specification). The

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limitation "discriminant loadings" (claim 27 and 28) is understood to refer to "the set of values derived from a set of control data that may be applied to a data set from an unclassified sample in order to project the unclassified sample into the dimensional space of the classification system" and interchangeable with the term "canonical coefficients" (page 24, lines 15-19 of the Specification).

No Claims Are Allowed.

EXAMINER INFORMATION

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 C.F.R. § 1.6(d)). The CM1 Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Channing S. Mahatan whose telephone number is (571) 272-0717. The Examiner can normally be reached on M-F (8:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

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USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify Applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables Applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Date:

July 8, 2004

Examiner Initials:

*CSM**Marianne P. Allen***MARIANNE P. ALLEN
PRIMARY EXAMINER***7/8/04**AU/631*